Office Action Summary	Application No.	Applicant(s)	
	09/847,172	BURROWS ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-40,54 and 59-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-40,54 and 59-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09182001, 06252003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/200942 and is a continuation-in-part of U.S. Application Serial Number 09/153,586, which claims the benefit of the filing date of provisional application 60/064,552 and 60/064,555.

Claims 1-36, 41-53 and 55-58 have been canceled.

New claims 79-82 have been added.

Claims 37-40, 54 and 59-82 are currently pending.

Election/Restrictions

Applicant's election with traverse of myelin basic protein as the antigen species in the reply filed on February 5, 2003 is acknowledged. The traversal is on the ground(s) that the method of the claims is generic and is not dependent upon the antigenic peptide chosen.

Upon further review, the **species requirement is hereby withdrawn**.

Claims **37-40, 54 and 59-82 are the subject of examination** in the present Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 37-40, 54 and 59-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Briefly, the claims are broadly drawn to a method for reducing an immune response in a subject [claims 37-40, 69-80] and treating a disease caused by antigen-specific T cells [claims 54, 59-68, 81-82]. All claims require the administration to a subject a composition comprising an MHC class II construct having an $\alpha 1$ domain and a $\beta 1$ domain, but lacking an $\alpha 2$ domain and a $\beta 2$ domain. Claim 37 further requires a subsequent challenge with an antigenic determinant and claim 63 (dependent upon claim 54) requires that an antigenic determinant is linked to the MHC class II construct. The claims are not enabled in several regards.

First, there is no requirement in the claims that the MHC class II construct is specific for the

antigenic determinant. It has been well-established in the art that in order to effect or affect an immune response, an MHC class II molecule must be specific for the peptide fragment so that the peptide can be bound within the binding groove of the MHC class II complex or (in the case of a single-chain peptide) construct. Without such specific binding of the antigenic fragment, the MHC class II/peptide complex cannot be properly formed and cannot be recognized or bound by T cells specific for the antigenic determinant. Even when the antigenic determinant is covalently bound to the MHC class II molecule, unless there is specific recognition of the peptide by the MHC class II construct, the MHC class II peptide merely serves as a carrier protein in the same manner that ovalbumin (for example) would.

Second, the claims are drawn to the in vivo treatment of an immune response including (and specifically reciting in claims 59-61 and 69-71) various autoimmune diseases characterized by different disease etiologies and reactivities to various autoantigens. The effectiveness of treating a response to an autoantigen is dependent on several factors, the most critical of which is whether the therapy can be used to treat an ongoing autoimmune response or whether it is only effective prophylactically (Tisch et al, Tisch, R et al. Proc. Nat. Acad. Sci. (USA). [1994] 91:437-438; U on form PTO-892, page 437, column 2, last paragraph in particular). Typically, an autoimmune disease is diagnosed only after significant tissue damage has already occurred. Administration of antigen after pathogenic T cells have been activated may have an exacerbating effect on the disease, rather than a tolerogenic one. Another problem during the treatment of autoimmune diseases is determinant spreading during the course of the disease. The Tisch et al reference also teaches that "the high degree of specificity required for the process of clonal deletion/anergy may be limiting when dealing with diseases such as MS, IDDM, and RA, in which there are responses to several autoantigens [...] and the critical inciting autoantigen(s) is not known" (page 437, third full paragraph of column 3 in particular). The breadth of Applicant's claim is such that it recites a composition for the treatment of unrelated autoimmune diseases with a fragment of the MHC class II extracellular domain, as there is no requirement to match the MHC class II molecule to either the determinant or disease. The specification demonstrates only that the MHC peptides and antigenic determinants of the invention were capable of stimulating T cell lines and T cells derived from the peripheral blood lymphocytes of human subjects wherein the T cells were selected to be specific for the antigenic determinant. The specification does not show that the peptides disclosed in the specification were able to inhibit the autoimmune reactivity of any T cells, either those of T cell lines or patient-derived. Furthermore, the specification does not address the phenomenon of determinant spreading and requires that the antigenic determinant .

In view of the nature of the invention, the state of the art, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

Conclusion

3. No claim is allowed.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
September 22, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
9/29/04